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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/403,213	06/22/2000	Matheus Hubertus Maria Noteborn	LEBV.004.01U	6984

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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 02/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/403,213	NOTEBORN ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-16,22,25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *2,5 and 7* is/are allowed.

6)☒ Claim(s) *1,4,6,8-16,22 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Non-Final Rejection

Claims 1, 2, 4-16, 22 and 25 are pending.

Applicants' traversal, the amendment to claims 22 and 25 in paper filed on 12/13/03 is acknowledged and considered.

The indicated allowability of claims 1, 4, 6, 8-11 is withdrawn in view of the newly discovered reference(s) to US 5,592,002. Rejections based on the newly cited reference(s) follow.

Priority

Applicants request clarification for the assertion on page 2 of the office action mailed on that 08/454,121 application was filed five months after the 08/482,161 application and thus the priority claim was inappropriate.

The US filing date for 08/454,121 is 11/30/95 and not 7/19/94 as asserted by applicants. The filing date 7/19/94 is for PCT/NL94/00168. The US filing date for 08/482,161 is 6/7/1995. In view of the US filing dates for both applications, US application '121 was filed 5 months after the filing date of US application '161 and is inappropriate. It is inappropriate because '161 cannot be a CIP of an application ('121) that was filed after '161.

Specification

The disclosure is objected to because of the following informalities: the SEQ ID NOs: for the sequences on page 19, lines 5, 7, and 14 are missing. The sequences are listed on the CRF. See MPEP 2422, 37 CFR 1.821(d).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22 and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using a recombinant gene delivery vehicle comprising a nucleic acid sequence encoding a chicken anemia virus (CAV) VP3 and/or VP2 proteins operatively linked to a promoter in a method for inducing apoptosis in a tumor of a mammal, does not reasonably provide enablement for using a recombinant gene delivery vehicle comprising a nucleic acid sequence encoding CAV VP3 and/or VP2 proteins not operatively linked to a promoter in the claimed method. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

With respect to claims 22 and 25, the claims embrace a method of inducing apoptosis in a mammalian tumor by directly administering to a tumor of a mammal the gene delivery vehicle of claim 1 or claim 6. The specification provides sufficient guidance for one skilled in the art to

make and use a recombinant gene delivery vehicle, which expresses CAV VP2 protein and/or CAV VP3 protein operatively linked to a promoter. However, the specification fails to provide sufficient guidance or evidence for one skilled in the art to make and use a recombinant gene delivery vector, which express VP2 and/or VP3 that is not operatively linked to any promoter in the gene delivery vehicle. The teachings in the specification are directed to using a promoter to express the CAV gene product(s). See pages 10 and 12 and Figure 2. The as-filed specification provides sufficient guidance and/or evidence for how to make and use vectors comprising a promoter operatively linked to a recombinant nucleic acid molecule encoding a CAV protein VP3 and/or VP2 to direct VP3 and/or VP2 expression, however the claims do not recite such a structural limitation. Thus, to the extent the claims fail to recite distinguishing features to commensurate with the level of guidance presented, the claims are not considered enabled.

In conclusion, the as-filed specification and claims coupled with the art of record at the time the invention was made provide enablement for a recombinant gene delivery vehicle comprising a nucleic acid sequence encoding a chicken anemia virus (CAV) VP3 and/or VP2 proteins operatively linked to a promoter in a method for inducing apoptosis in a tumor of a mammal. However, the rest of the disclosure encompassing any gene delivery vehicle comprising a promoter not operatively linked to a nucleotide sequence from the vehicle is not considered enabled for the reasons set forth above. Given that making a recombinant gene delivery vehicle, which expresses VP2 and/or VP3 protein(s) comprising a promoter not operatively linked to a nucleotide sequence in the vehicle was unpredictable at the time the invention was made, and given the lack of sufficient guidance for producing the claimed gene delivery vehicle, one skilled in the art would have to engage in a large quantity of

experimentation in order to practice the full scope of the claimed invention based on the applicants' disclosure.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 4, and 6 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 5, 10 and 11 of U.S. Patent No. 5,952,002. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims from the instant application and US Patent '020 are directed to a vector comprising a recombinant DNA encoding a polypeptide comprising SEQ ID NO: 5 (CAV VP2 protein) or a composition comprising CAV DNA encoding VP2 and VP3.

Claims 1, 8, 9, 10, and 11 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 5, 10 and 11 of U.S. Patent No. 5,952,002 in view of Mason et al. (US Patent No. 5,643,770, filed with a previous office action mailed 8/29/02).

The claims from US patent '002 are directed to a vector comprising a recombinant DNA encoding CAV protein VP3 and/or VP2. The difference between claims of US Patent '002 and the instant application is that the instant application claims a viral vector, wherein the viral vector is a replication defective retroviral vector or a replication defective adenoviral vector. However, Mason teaches that replication defective adenoviral and replication defective retroviral vectors were well known in the art for use in transducing cells (column 4, lines 10-21). One of ordinary skill in the art would have motivated to combine the teaching of Noteborn with Mason to make and use replication defective adenoviral or retroviral vectors comprising a nucleotide sequence encoding CAV protein VP2 and/or VP3 and a retroviral packaging cell line using PA-317. One of ordinary skill in the art would have been motivated to make and use either replication defective viral vector because Mason teaches that these vectors are efficient at transducing cells. Therefore, the claims of the instant application and '002 in view of Mason are obvious variants of one another.

Claims 1, 6, 12, and 13 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 5, 10 and 11 of U.S. Patent No. 5,952,002 in view of Panicali et al (US 5,656,465).

The claims from US patent '002 are directed to a vector comprising a recombinant DNA encoding CAV protein VP3 and VP2. The difference between claims of US patent '002 and the instant application is that the instant application claims a vector, which additionally comprises at least one target molecule that is reactive with a tumor cell surface receptor. However, Panicali teaches a vector comprising a gene encoding a toxin fused to a polypeptide that directs the toxin

to a target, such as a tumor cell (column 5, lines 20-65). One of ordinary skill in the art would have been motivated to fuse a polypeptide to the VP2 and VP3 gene product to target a tumor cell to increase the delivery of the vector to a tumor cell. Therefore, the claims of the instant application and US Patent '002 in view of Panicali are obvious variants of one another.

Claims 1, 6, 12, 13, 14, 15, and 16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 5, 10 and 11 of U.S. Patent No. 5,952,002 taken with Panicali et al (US 5,656,465) in view further view of Mason et al. (US Patent No. 5,643,770).

The claims from US patent '002 are directed to a host cell comprising a vector comprising a recombinant DNA encoding CAV protein VP3 and VP2. The difference between claims of US patent '002 and the instant application is that the instant application claims a host cell comprising a vector comprising a recombinant DNA encoding CAV protein VP3 and VP2 further comprising at least one target molecule and the host cell is PA-317.

However, Panicali teaches a vector comprising a gene encoding a toxin fused to a polypeptide that directs the toxin to a target, such as a tumor cell (column 5, lines 20-65). In addition, Mason teaches retroviral vectors and producing a retroviral packaging cell line using PA-317 cells (column 15, lines 21-33). Mason teaches that retroviral vectors are efficient at transducing cells (column 4, lines 10-21).

One of ordinary skill in the art would have motivated to combine the teaching of Noteborn with Panicali in further view of Mason to make and use retroviral vectors comprising a nucleotide sequence encoding CAV protein VP2 and/or VP3 and a target molecule. One of

ordinary skill in the art would have been motivated to fuse a polypeptide to the VP2 and VP gene product to target a tumor cell to increase the delivery of the vector to a tumor cell.

In addition, one of ordinary skill in the art would have been motivated to combine the teaching of Noteborn with Panicali in further view of Mason to use a retroviral packaging cell line, PA-317 to produce retroviral vectors. One of ordinary skill in the art would have been motivated to make and use the packaging cell to make replication retroviral vector because Mason teaches that these vectors are efficient at transducing cells.

Therefore, the claims of the instant application and '002 in view of Panicali in further of Mason are obvious variants of one another.

Response to Arguments

Applicant's arguments, filed 12/13/03, with respect to claim objection have been fully considered and are persuasive. The objection of claims 22 and 25 has been withdrawn because of the amendment to claims 22 and 25.

Applicant's arguments, filed 12/13/03, with respect to the double patenting rejection over US 6,472,142 have been fully considered and are persuasive. The rejection of claims 22 and 25 has been withdrawn because of the terminal disclaimer.

Applicant's arguments, filed 12/13/03, with respect to the double patenting rejection over US 5,981,502 have been fully considered and are persuasive. The rejection of claims 22 and 25 has been withdrawn because of the terminal disclaimer.

Applicant's arguments, filed 12/13/03, with respect to the double patenting rejection over US 6,162,461 have been fully considered and are persuasive. The rejection of claims 22 and 25 has been withdrawn because of the terminal disclaimer.

Conclusion

Claims 2, 5, and 7 are in condition for allowance because the claims are free of the prior of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, SPE - Art Unit 1635, can be reached at (571) 272-0760.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER

Brian Whiteman
Patent Examiner, Group 1635